IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

Ravgen, Inc., Plaintiff, v. Myriad Genetics, Inc., and Myriad Women's Health, Inc., Defendants.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Ravgen, Inc. ("Ravgen"), for its Complaint against Defendants Myriad Genetics, Inc. ("Myriad") and Myriad Women's Health, Inc. ("MWH") (collectively "Defendants"), hereby alleges as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 7,727,720 (the "'720 Patent") and 7,332,277 (the "'277 Patent") (collectively the "Patents-in-Suit"), arising under the Patent Laws of the United States, 35 U.S.C. §§ 271 *et seq*.

THE PARTIES

2. Plaintiff Ravgen is a Delaware corporation with its principal place of business at 9241 Rumsey Rd., Columbia, MD 21045. Ravgen is a pioneering diagnostics company that focuses on non-invasive prenatal testing. Ravgen has spent millions of dollars researching and developing novel methods for the detection of cell-free DNA to replace conventional, invasive procedures. Ravgen's innovative cell-free DNA technology has various applications, including

non-invasive prenatal and other genetic testing. Those efforts have resulted in the issuance of several patents, including the Patents-in-Suit.

3. Defendant Myriad is a company organized and existing under the laws of the State of Delaware, with its principal place of business at 320 Wakara Way, Salt Lake City, Utah 84108. (Ex. 7 (Myriad Genetics Form 10-K, June 30, 2020) at 1.) Myriad has appointed The Corporation Trust Company, Corporation Trust Center 1209 Orange Street, Wilmington, Delaware 19801 as its agent for service of process. (Ex. 8 (State of Delaware Entity Status for Myriad Genetics, Inc.).)

4. Defendant MWH is a company organized and existing under the laws of the State of Delaware, with its principal place of business at 180 Kimball Way, South San Francisco, California 94080. (Ex. 9 (https://myriadwomenshealth.com/about-us/); Ex. 7 (Myriad Genetics Form 10-K, June 30, 2020) at 103.) MWH has appointed The Corporation Trust Company, Corporation Trust Center 1209 Orange Street, Wilmington, Delaware 19801 as its agent for service of process. (Ex. 10 (State of Delaware Entity Status for Myriad Women's Health, Inc.).) MWH is a wholly-owned subsidiary of Myriad Genetics. (Ex. 7 (Myriad Genetics Form 10-K, June 30, 2020) at 103.)

5. Defendants, themselves and/or through their subsidiaries and affiliates, make, use, and commercialize noninvasive prenatal tests that utilize circulating cell-free DNA (cfDNA) to screen for and detect genetic abnormalities, such as aneuploidy of chromosomes, marketed under the tradenames "Prequel," "Prelude," and "Informed."

6. Defendants have offered and marketed tests under the Prequel, Prelude, and Informed tradenames throughout the United States, including without limitation through the website, www.myriadwomenshealth.com. (*See generally* Ex. 11 (https://myriadwomenshealth.com/provider-prequel/).)

JURISDICTION AND VENUE

7. Ravgen incorporates by reference paragraphs 1–6.

8. This action arises under the patent laws of the United States, including 35 U.S.C. §§ 271 *et seq*. The jurisdiction of this Court over the subject matter of this action is proper under 28 U.S.C. §§ 1331 and 1338(a).

9. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391(b), (c), and 1400(b). Defendants are entities organized under the laws of Delaware and reside in Delaware for purposes of venue under 28 U.S.C. § 1400(b). Defendants conduct business in Delaware, at least by offering for sale and selling products and services through their websites, which are accessible in Delaware. Defendants have also committed and continue to commit acts of infringement in this District.

10. This Court has personal jurisdiction over Defendants because Defendants conduct business in Delaware by at least offering for sale or selling products and services through their websites, which are accessible in Delaware, and because infringement has occurred and continues to occur in Delaware.

11. Personal jurisdiction also exists over Defendants because they are entities organized under the laws of Delaware.

BACKGROUND OF THE INVENTION

12. Dr. Ravinder S. Dhallan is the founder of Ravgen, Inc. and the inventor of several patents in the field of detection of genetic disorders, including chromosomal abnormalities and mutations. Ravgen's mission is to provide state of the art genetic testing that will enrich the lives of its patients. For example, through the use of its novel techniques in non-invasive prenatal diagnostic testing, Ravgen gives patients the knowledge they need to prepare for their pregnancies and treat diseases at an early stage.

13. Prior to founding Ravgen, Dr. Dhallan was a board-certified emergency room physician. Between starting medical school at Johns Hopkins University and shortly after his residency at Mass General (Harvard University School of Medicine), Dr. Dhallan and his wife suffered three miscarriages. At that time, the prenatal diagnostic testing procedures available included (a) non-invasive techniques with low sensitivity and specificity, and (b) tests with higher sensitivity and specificity that were highly invasive and therefore associated with a risk for loss of pregnancy. After discovering the limitations on the available techniques for prenatal testing, Dr. Dhallan made it his mission to invent an improved prenatal diagnostic exam—one that was both non-invasive and accurate. In September of 2000, Dr. Dhallan founded Ravgen (which stands for "Rapid Analysis of Variations in the GENome") to pursue that goal.

14. Prior to Ravgen's inventions, scientists had recognized the need for a genetic testing technique that used "cell-free" or "free" fetal DNA circulating in maternal blood. A technique that relied on circulating free fetal DNA would require only a simple blood draw from the mother and would therefore be an improvement over invasive diagnostic tests.

15. However, at that time, the use of free fetal DNA for detecting chromosomal abnormalities was limited by the low percentage of free fetal DNA that could be recovered from a sample of maternal blood using existing techniques. (*See, e.g.*, Ex. 12 (Y.M. Dennis Lo et al., *Presence of Fetal DNA in Maternal Plasma and Serum*, 350 THE LANCET 768-75 (1997), https://doi.org/10.1016/S0140-6736(97)02174-0).) Dr. Dhallan recognized that a method that could increase the percentage of free fetal DNA relative to the free maternal DNA in a sample was necessary to the development of an accurate, non-invasive prenatal diagnostic test.

16. After substantial research, Dr. Dhallan conceived that including an agent that impedes cell lysis (disruption of the cell membrane) if cells are present during sample collection,

shipping, handling, and processing would permit the recovery of a larger percentage of cell-free fetal DNA (relative to the cell-free maternal DNA in a sample). Dr. Dhallan hypothesized that this new approach would decrease the amount of maternal cell lysis and therefore lower the amount of cell-free maternal DNA in the sample, thereby increasing the percentage of cell-free fetal DNA. He developed a novel method for processing cell-free fetal DNA that involved the addition of an agent that impedes cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—to maternal blood samples coupled with careful processing protocols. With that novel method, Dr. Dhallan was able to increase the relative percentage of cell-free fetal DNA in the processed sample.

17. Having successfully increased the relative percentage of cell-free fetal DNA recovered, Dr. Dhallan next addressed the challenge of distinguishing between the cell-free maternal and cell-free fetal DNA in a sample in order to determine whether a chromosomal abnormality is present in the fetal DNA. Prior to Ravgen's inventions, known methods for detecting fetal chromosomal abnormalities were time-consuming and burdensome. Many required amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product in a sample. Dr. Dhallan developed an alternate method that greatly increased the efficiency of this process by taking advantage of the variation of base sequences among different individuals (including a mother and fetus) ("alleles") at particular positions ("loci") on chromosomes. The term "allele" refers to an alternate form of a gene, or a non-coding region of DNA that occurs at a particular locus on a chromosome. The alleles present at certain loci on chromosomes (including, for example, "single nucleotide polymorphisms" or "SNPs") vary between different individuals. At such a locus, a fetus may therefore inherit an allele from its father that differs from the alleles present at that locus on its mother's chromosome. Dr. Dhallan

developed a novel method for quantifying the allelic ratio at such a locus (or loci) of interest in a sample comprising maternal and fetal cell-free DNA in order to detect whether a fetal chromosomal abnormality was present in the fetal DNA of the sample, without requiring physical separation of the fetal from the maternal cell-free DNA.

18. Dr. Dhallan understood that his breakthroughs laid the foundation for the development of accurate non-invasive prenatal diagnostic tests. For example, he published a paper in the *Journal of the American Medical Association* (*JAMA*) in 2004, explaining that "the methods described herein for increasing the percentage of cell-free fetal DNA provide a solid foundation for the development of a noninvasive prenatal diagnostic test." (Ex. 13 at 1119 (R. Dhallan et al., *Methods to Increase the Percentage of Free Fetal DNA Recovered from the Maternal Circulation*, 291 JAMA 1114–19 (2004), https://doi.org/10.1001/jama.291.9.1114).)

19. *JAMA* also ran an editorial alongside Dr. Dhallan's article in 2004, recognizing the significance of his inventions to applications in prenatal genetic diagnosis and cancer detection and surveillance:

> In this issue of THE JOURNAL, the findings reported in the study by Dhallan and colleagues on enhancing recovery of cell-free DNA in maternal blood have major clinical implications. Developing a reliable, transportable technology for cell-free DNA analysis impacts 2 crucial areas—prenatal genetic diagnosis and cancer detection and surveillance. In prenatal genetic diagnosis, detecting a fetal abnormality without an invasive procedure (or with fewer invasive procedures) is a major advantage. Likewise in cancer surveillance (eg, in patients with leukemia), monitoring treatment without having to perform a bone marrow aspiration for karyotype also would be of great benefit.
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> With prospective studies focusing on clinical applications of these findings, profound clinical implications could emerge for prenatal diagnosis and cancer surveillance.

(Ex. 14 at 1135, 1137 (J.L. Simpson & F. Bischoff, *Cell-Free Fetal DNA in Maternal Blood: Evolving Clinical Applications*, 291 JAMA 1135–37 (2004), https://doi.org/10.1001/jama.291.9.1135).)

20. In 2007, Dr. Dhallan published a second journal article in *The Lancet* that presented a study showcasing Ravgen's ability to use its novel technology to detect Down's syndrome using free fetal DNA in a maternal blood sample. (Ex. 15 (R. Dhallan et al., *A Non-Invasive Test for Prenatal Diagnosis Based on Fetal DNA Present in Maternal Blood: A Preliminary Study*, 369 THE LANCET 474–81 (2007), https://doi.org/10.1016/S0140-6736(07)60115-9).) Dr. Dhallan's peers at *The Lancet* also recognized that his innovative test "opens a new era in prenatal screening." (*See* Ex. 16 (A. Benachi & J.M. Costa, *Non-Invasive Prenatal Diagnosis of Fetal Aneuploidies*, 369 THE LANCET 440–42 (2007), https://doi.org/10.1016/S0140-6736(07)60116-0).)

21. Dr. Dhallan's publications received worldwide press coverage, from outlets such as CNN, BBC, and Washington Post. (*See* Ex. 17 (L. Palmer, *A Better Prenatal Test?*, CNN MONEY (Sept. 12, 2007), https://money.cnn.com/2007/09/07/smbusiness/amniocentesis.fsb/index.htm); Ex. 18 (*Hope for Safe Prenatal Gene Test*, BBC NEWS, Feb 2, 2007, http://news.bbc.co.uk/2/hi/health/6320273.stm); Ex. 19 (A. Gardner, *Experimental Prenatal Test Helps Spot Birth Defects*, WASH. POST (Feb. 2, 2007), https://www.washingtonpost.com/wp-dyn/content/article/2007/02/02/AR2007020200914.html).)

22. The Patents-in-Suit resulted from Dr. Dhallan's years-long research at Ravgen to develop these innovative new methods for detecting genetic disorders.

PATENTS-IN-SUIT

23. Ravgen incorporates by reference paragraphs 1–22.

24. The ’277 Patent, entitled “Methods For Detection Of Genetic Disorders,” was duly and legally issued by the United States Patent and Trademark Office on February 19, 2008. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the ’277 Patent is attached hereto as Exhibit 1.

25. Ravgen is the exclusive owner of all rights, title, and interest in the ’277 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the ’277 Patent. (*See* Ex. 3.)

26. The ’720 Patent, entitled “Methods For Detection Of Genetic Disorders,” was duly and legally issued by the United States Patent and Trademark Office on June 1, 2010. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the ’720 Patent is attached hereto as Exhibit 2.

27. Ravgen is the exclusive owner of all rights, title, and interest in the ’720 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the ’720 Patent. (*See* Ex. 4.)

28. The ’277 Patent is directed to, among other things, novel methods used in the detection of genetic disorders. For example, claim 81 of the ’277 Patent recites:

> A method for preparing a sample for analysis comprising isolating free fetal nucleic acid from a the sample, wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.

29. The ’720 Patent is directed to novel methods for detecting a free nucleic acid in a sample. For example, claim 1 of the ’720 Patent recites:

> A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is

> selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

30. The Patents-in-Suit are directed to unconventional, non-routine techniques for preparing and analyzing extracellular circulatory DNA, including for the detection of genetic disorders. The Patents-in-Suit explain that, *inter alia*, the inventions claimed therein overcame problems in the field—for example, that the low percentage of fetal DNA in maternal plasma makes using the DNA for genotyping the fetus difficult—with a novel and innovative solution—the addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample, which increase the percentage of cell-free DNA available for detection and analysis:

> The percentage of fetal DNA in maternal plasma is between 0.39-11.9% (Pertl, and Bianchi, *Obstetrics and Gynecology* 98: 483-490 (2001)). **The majority of the DNA in the plasma sample is maternal, which makes using the DNA for genotyping the fetus difficult**. However, methods that increase the percentage of fetal DNA in the maternal plasma allow the sequence of the fetal DNA to be determined, and allow for the detection of genetic disorders including mutations, insertions, deletions, and chromosomal abnormalities. **The addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample can increase the relative percentage of fetal DNA.** While lysis of both maternal and fetal cells is inhibited, the vast majority of cells are maternal, and thus by reducing the lysis of maternal cells, there is a relative increase in the percentage of free fetal DNA.

(Ex. 1 (’277 Patent) at 32:24–39; Ex. 2 (’720 Patent) at 33:31–46 (emphases added).)

31. The Patents-in-Suit teach that the benefit of Dr. Dhallan’s discovery, an increase in the relative percentage of cell-free DNA, is realized by performance of the claimed method, including through the inclusion of an agent that inhibits the lysis of the cells in a sample:

> An overall increase in fetal DNA was achieved by reducing the maternal cell lysis, and thus, reducing the amount of maternal DNA present in the sample. In this example, formaldehyde was used to prevent lysis of the cells, however any agent that prevents the lysis of cells or increases the structural integrity of the cells can be used.

> Two or more than two cell lysis inhibitors can be used. The increase in fetal DNA in the maternal plasma allows the sequence of the fetal DNA to be determined, and provides for the rapid detection of abnormal DNA sequences or chromosomal abnormalities including but not limited to point mutation, reading frame shift, transition, transversion, addition, insertion, deletion, addition-deletion, frame-shift, missense, reverse mutation, and microsatellite alteration, trisomy, monosomy, other aneuploidies, amplification, rearrangement, translocation, transversion, deletion, addition, amplification, fragment, translocation, and rearrangement.

(Ex. 1 ('277 Patent) at 91:44–60; Ex. 2 ('720 Patent) at 92:10–26.)

32. For example, during the prosecution of the '720 Patent at the Patent and Trademark Office, Ravgen explained that the innovative concept of using agents that inhibit cell lysis during cell-free DNA detection and analysis is recited by the claimed methods of the '720 Patent, including in claim 1:

> Applicant has discovered that the addition of a cell lysis inhibitor to a sample prior to detecting the presence of free nucleic acid can ***significantly and unexpectedly*** increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample.
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> The methods disclosed in claims 1-8, 21-23, and 26 serve a long-felt need in the medical community, and provide unexpected results, and are therefore non-obvious.

(Ex. 5 ('720 File History, June 2, 2009 Response to Office Action) at 12, 14 (emphasis added).)

33. The inventive concept of the Patents-in-Suit of including an agent that inhibits cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—with a sample represented a significant improvement in the preparation of samples used for non-invasive testing, including non-invasive prenatal testing to unmask previously undetectable fetal genetic traits. At the time of the invention, it would not have been routine or conventional to add an agent that inhibits cell lysis to a sample to increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample. In fact, as described above, that inventive concept was

recognized by Dr. Dhallan's peers as "an important step in improving detection of cell-free DNA." (Ex. 14 at 1137.)

34. The '277 Patent is further directed to an unconventional, non-routine method of detecting fetal chromosomal abnormalities which involves "quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA." (Ex. 6 ('277 File History, May 30, 2007 Response to Office Action) at 30.) For example, claim 1 of the '277 Patent recites:

> A method for detecting the presence or absence of a fetal chromosomal abnormality, said method comprising: quantitating a ratio of the relative amounts of alleles at a heterozygous locus of interest in a mixture of template DNA, wherein said mixture comprises maternal DNA and fetal DNA, and wherein said mixture of maternal DNA and fetal DNA has been obtained from a sample from a pregnant female, and further wherein said heterozygous locus of interest has been identified by determining the sequence of alleles at the locus of interest, and wherein said ratio indicates the presence or absence of a fetal chromosomal abnormality.

35. The '277 Patent explains that this claimed method represented a significant improvement over prior art methods of detecting fetal chromosomal abnormalities, many of which were costly, time-consuming, and burdensome because they either required the amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product. (Ex. 1 at 66:14-20.) By contrast, the claimed "ratio" method of the '277 Patent only requires sequencing of discrete "loci of interest" (such as "single nucleotide polymorphisms," or "SNPs") from the collected DNA sample. (*Id.* at 34:63-35:37 ("In fact, it is an advantage of the invention that primers that copy an entire gene sequence need not be utilized. . . . There is no advantage to sequencing the entire gene as this can increase cost and delay results. Sequencing only the desired bases or loci of interest maximizes the overall efficiency of the method because it allows for the sequence of the maximum number of loci of interest to be determined in the fastest amount of time and with minimal cost."); *Id.* at 35:28-37.)

36. During the prosecution of the ’277 Patent at the Patent and Trademark Office, Ravgen gave the following example of an implementation of the claimed “ratio” method:

> Applicants have invented a method for detecting the presence or absence of a fetal chromosomal abnormality, wherein the method comprises, inter alia, quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA.
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> [R]atios were calculated at both chromosomes 13 and 21 in a heterogeneous mixture of 75% Down syndrome DNA and 25% maternal DNA. Single nucleotide polymorphisms were analyzed wherein the maternal genome was homozygous for one allele at a specific genetic site and the Down syndrome DNA was heterozygous at the same genetic site. If at a certain site, the maternal genome contains an adenine at both copies of chromosome 13, and the Down syndrome genome is comprised of one chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.60 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.25 + 0.25 maternal A alleles).
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> On the other hand, if at a certain genetic site on chromosome 21, the maternal genome contains an adenine at both copies of chromosome 21, and the Down syndrome genome is comprised of two chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.375 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.75 Down syndrome A allele + 0.25 + 0.25 (maternal A alleles). Thus, the methods described in the present application detect chromosomal abnormalities using a method that comprises, inter alia, quantitating a ratio of alleles in a heterogeneous mixture of DNA, wherein the ratio represents alleles from more than one individual.

(Ex. 6 at 30.)

DEFENDANTS’ INFRINGING ACTIVITIES

37. Ravgen incorporates by reference paragraphs 1–36.

A. The Accused Myriad Prenatal Screens

38. In or around September 2014, Counsyl, Inc. (“Counsyl”) began offering a commercial non-invasive prenatal test for detecting fetal chromosomal abnormalities. (*See* Ex. 20

at 5 (https://blog.myriadwomenshealth.com/2017/10/24/a-decade-of-counsyl/).) On information and belief, that non-invasive prenatal test was the "Informed Pregnancy Screen." In 2017, Counsyl renamed the Informed Pregnancy Screen product to "Prelude Prenatal Screen." (*See* Ex. 21 (https://www.businesswire.com/news/home/20170719005438/en/Counsyl-Unveils-Updated-Names-for-its-Portfolio-of-Genetic-Testing-Products-and-Services); Ex. 22 (https://blog.myriadwomenshealth.com/2017/06/28/newnames/).)

39. On or around July 31, 2018, Myriad acquired Counsyl and merged Counsyl with Myriad Preventative Care to form MWH. (*See* Ex. 23 (https://blog.myriadwomenshealth.com/2018/09/10/counsyl-transitioning-to-myriad-womens-health-inc/).) Since Myriad's acquisition of Counsyl, the Prelude Prenatal Screen has been renamed to "Prequel Prenatal Screen." (Ex. 24 at 1 (https://myriadwomenshealth.com/wp-content/uploads/2020/06/Prequel-Sample-Report-Trisomy-21-Positive-0119.pdf) ("The Counsyl Prelude™ Prenatal screen has been renamed the Myriad Prequel™ Prenatal screen."); Ex. 25 at 2658 (Katherine Johansen Taber, *et al.*, *Inaccuracies and shortcomings in "Adherence of cell-free DNA noninvasive prenatal screens to ACMG recommendations"*, 21 GENETICS IN MEDICINE 2658, 2658 (2019)) ("We cite three examples regarding Prelude (now Prequel, Myriad Women's Health [MWH]) . . . .").)

40. On information and belief, Myriad has offered the Prequel Prenatal Screen since at least February 11, 2019. (Ex. 26 (https://investor.myriad.com/news-releases/news-release-details/myriad-announces-prequeltm-prenatal-screen-expanded-aneuploidy).)

41. On information and belief, the "Informed Pregnancy Screen," the "Prelude Prenatal Screen," and the "Prequel Prenatal Screen" (collectively, the "Myriad Prenatal Screens") at least require the same methods of sample collection, preparation, and processing to detect fetal

chromosomal abnormalities. The Myriad Prenatal Screens have been offered by Defendants since at least September 2014.

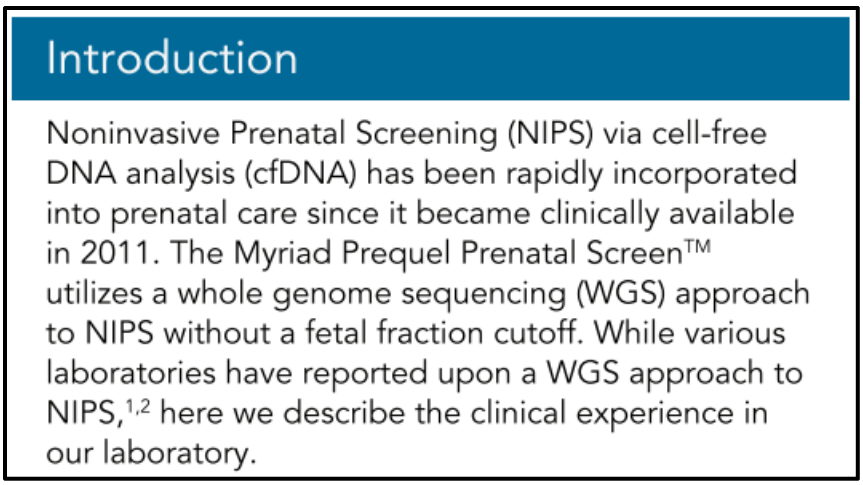
42. The Myriad Prenatal Screens are "noninvasive prenatal screen[s] that use[] cell-free DNA (cfDNA) to determine if a pregnancy is at an increased risk for common chromosome abnormalities, such as Down syndrome." (Ex. 11 at 3 (https://myriadwomenshealth.com/provider-prequel/).) The Myriad Prenatal Screens require a sample of maternal blood. (Ex. 27 (https://myriadwomenshealth.com/patient-prequel/) ("All we need is a simple blood draw from your arm . . . .").)

43. The Myriad Prenatal Screens require samples containing an agent that inhibits cell lysis. For example, MWH's website instructs medical professionals to use a "Streck tube" as the container for the test specimen requirements. (Ex. 28 (https://myriadwomenshealth.com/how-to-10ml-blood/).); *see also* Ex. 29 (https://help.myriadwomenshealth.com/s/article/000016237) (Question: "How are samples collected for the Prequel Prenatal™ Screen?" Answer: "A sample is collected from a pregnant patient who is at least 10 weeks . . . into her pregnancy . . . . Specifically, Myriad Women's Health ***requires one 10mL Streck tube*** . . . .").) Myriad's requisition form for the Myriad Prenatal Screens instructs to "[u]se (One) 10mL STRECK." (Ex. 30 (Preconception/Prenatal Requisition Form); *see also* Ex. 24 (Sample Report) ("Sample Type: Streck Cell-Free DNA Blood Tube").) On information and belief, "Streck tube" refers to the Streck Cell-Free DNA Blood Collection Tube ("BCT").

44. The Streck Cell-Free DNA BCT includes an agent that inhibits cell lysis. A Streck Cell-Free DNA BCT "stabilizes nucleated blood cells. The unique preservative ***limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA***. Cell-Free DNA BCT has also been demonstrated to minimize the degradation of circulating tumor cells (CTCs). By ***limiting***

cell lysis, the specialized chemistry provides sample integrity during storage, shipping and handling of blood samples. Cell-free DNA and gDNA are stable for up to 14 days at 6 °C to 37 °C. CTCs are stable for up to 7 days at 15 °C to 30 °C." (Ex. 31 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

45. In processing the Myriad Prenatal Screens, Defendants isolate cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and then analyze the isolated fetal cfDNA to detect chromosomal abnormalities as shown in Defendants' product documentation and a number of Myriad-funded scientific studies. The Myriad Prenatal Screens are a "Noninvasive Prenatal Screening" ("NIPS") that analyzes cell-free DNA using a "whole genome sequencing" ("WGS") approach.



(Ex. 32 (https://s3.amazonaws.com/static.counsyl.com/website/PDFs/posters/12.+Avoiding+Unnecessary+Trade-Offs+Clinical+Experience+for+a+Noninvasive+Prenatal+Screen.pdf) ("All authors are employees of Myriad Genetics.").) "NIPS directly interrogates cfDNA extracted from maternal plasma . . . ." (Ex. 33 at 334 (Dale Muzzey, *et al.*, *Noninvasive prenatal screening for patients with high body mass index: Evaluating the impact of a customized whole genome sequencing workflow on sensitivity and residual risk*, 40 PRENATAL DIAGNOSTICS 333, 334 (2020).) The

Myriad Prenatal Screens then analyze the extracted cfDNA to screen for fetal aneuploidy of chromosomes at MWH's laboratory. (*Id.*; Ex. 32 (https://s3.amazonaws.com/static.counsyl.com/website/PDFs/posters/12.+Avoiding+Unnecessary+Trade-Offs+Clinical+Experience+for+a+Noninvasive+Prenatal+Screen.pdf) ("Chromosome analysis results were reported as no aneuploidy detected ("negative"), aneuploidy detected ("positive"), or aneuploidy suspected (also "positive"); Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/) ("For Prequel, the patient will contact Client Services to discuss blood collection options and the phlebotomist will send the specimen to Myriad for processing.").)

B. Defendants' Knowledge Of The Ravgen Patents

46. The Patents-in-Suit claim advancements in the genetic testing industry in which Defendants actively participate and are widely acclaimed as breakthroughs in genetic testing. On information and belief, Defendants have been aware of the Patents-in-Suit and the fact that performance of the Defendants' cell-free DNA tests, including the Myriad Prenatal Screens, practice the claimed inventions of those patents since at least the launch date of each of the infringing products.

47. Defendants have been and are assignees of a number of patents and patent applications that are related to subject matter similar to the Patents-in-Suit and that were filed after the Patents-in-Suit were published. On information and belief, in researching the patentability of their own patents, Defendants did, or at a minimum should have, become aware of the Patents-in-Suit.

48. The Patents-in-Suit and their corresponding patent application publications were cited, either by Defendants or by an examiner, during prosecution of Defendants' own patent

applications at the United States Patent and Trademark Office. As persons skilled in the art, Defendants, upon learning of, reviewing, and/or citing the Patents-in-Suit, knew or were willfully blind to the fact that their infringing products practiced the Patents-in-Suit.

49. Ravgen's '277 Patent was cited during the prosecution and in the specification of Defendants' U.S. Patent Application Publication No. 2010/0022406. (Ex. 36 (U.S. Patent Application Publication No. 2010/0022406).)

50. Additionally, to the extent Defendants were not aware of the Patents-in-Suit prior to 2018, Defendants became aware of the Patents-in-Suit when they completed the acquisition of Counsyl in 2018.

51. Despite their knowledge of the Patents-in-Suit and of their infringement of those patents, Defendants have continued to willfully infringe the Patents-in-Suit so as to obtain the significant benefits of Ravgen's innovations without paying compensation to Ravgen. For example, Defendants have continued to use the claimed methods in their Myriad Prenatal Screens without a license, and, on information and belief, have generated hundreds of millions of dollars in revenue from their infringement. Additionally, after becoming aware of the Patents-in-Suit, Defendants proceeded to commercialize the Myriad Prenatal Screens built on and including the claimed inventions of the Patents-in-Suit without entering into a license to the Patents-in-Suit.

COUNT I

(Infringement Of The '277 Patent)

52. Ravgen incorporates by reference paragraphs 1–51.

53. The '277 Patent is valid and enforceable.

54. Defendants have infringed, and continue to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making,

using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Defendants' Myriad Prenatal Screens.

55. As one example, Defendants infringe at least Claim 81 of the '277 Patent by using the Myriad Prenatal Screens. For example, use of the Myriad Prenatal Screens requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 33 at 334 (Dale Muzzey, *et al.*, *Noninvasive prenatal screening for patients with high body mass index: Evaluating the impact of a customized whole genome sequencing workflow on sensitivity and residual risk*, 40 PRENATAL DIAGNOSTICS 333, 334 (2020) ("NIPS directly interrogates cfDNA extracted from maternal plasma . . . . [This] study included 58,105 patients who underwent WGS-based NIPS over an 8-month period with the Prequel Prenatal Screen . . . .").);

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with maternal blood) (*see, e.g.*, Ex. 28 (https://myriadwomenshealth.com/how-to-10ml-blood/).); Ex. 29 (https://help.myriadwomenshealth.com/s/article/000016237) (Question: "How are samples collected for the Prequel Prenatal™ Screen?" Answer: "A sample is collected from a pregnant patient who is at least 10 weeks . . . into her pregnancy . . . . Specifically, Myriad Women's Health requires one 10mL Streck tube . . . .");

Ex. 31 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

56. Defendants have infringed, and continue to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Myriad Prenatal Screens either themselves and/or by directing and/or controlling the performance of the claimed steps by third-party laboratories performing the Myriad Prenatal Screens. For example, Defendants use the Myriad Prenatal Screens by collecting and analyzing samples sent to Defendants' laboratories for processing. (*See, e.g.*, Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/) ("For Prequel, the patient will contact Client Services to discuss blood collection options and the phlebotomist will send the specimen to Myriad for processing."); Ex. 35 (https://myriadwomenshealth.com/our-science/) ("As one of the pioneers in clinical next generation sequencing (NGS) and one of the largest sequencing facilities in the world, Myriad Women's Health's CLIA laboratory has tested over one million samples.").) On information and belief, Myriad has the right and the ability to direct and control the activities of MWH in several ways, including through Myriad's 100% ownership of MWH, through instituting programs and measures (such as policies or protocols) at MWH, and through interim instructions via at least Myriad's employees and/or officers who hold leadership roles at MWH. Further, MWH acts on behalf of Myriad, including when MWH performs tests on Myriad's behalf for Myriad's patients, or provides test results to health care providers and/or patients on Myriad's behalf.

57. In addition or in the alternative, Defendants have also induced infringement, and continue to induce infringement, of one or more claims of the '277 Patent under 35 U.S.C. § 271(b). Defendants actively, knowingly, and intentionally induce infringement of the '277 Patent by selling or otherwise supplying the Myriad Prenatal Screens with the knowledge and intent that third-party laboratories will use the Myriad Prenatal Screens supplied by Defendants to infringe the '277 Patent. Defendants act with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Myriad Prenatal Screens and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Myriad Prenatal Screens.

58. Defendants specifically intend and are aware that the ordinary and customary use of the Myriad Prenatal Screens would infringe the '277 Patent. For example, Defendants sell and provide the Myriad Prenatal Screens, which when used in their ordinary and customary manner intended and instructed by Defendants, infringe one or more claims of the '277 Patent, including at least claim 81. On information and belief, Defendants further provide product manuals and other instructional materials that cause their customers and partners to operate the Myriad Prenatal Screens for their ordinary and customary use. (*See*, *e.g.*, Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/); Ex. 28 (https://myriadwomenshealth.com/how-to-10ml-blood/).) Defendants accordingly induce third parties to use the Myriad Prenatal Screens in their ordinary and customary way to infringe the '277 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '277 Patent.

59. In addition or in the alternative, Defendants contribute to the infringement by third parties, such as health care providers or laboratories, of one or more claims of the '277 Patent

under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the Myriad Prenatal Screens, knowing that those products constitute a material part of the inventions of the ’277 Patent, knowing that those products are especially made or adapted to infringe the ’277 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

60. Defendants have had knowledge of and notice of the ’277 Patent and their infringement since at least the launch date of each of the infringing products.

61. Defendants’ infringement of the ’277 Patent has been, and continues to be, willful and deliberate since at least the launch date of each of the infringing products.

62. Ravgen has been and continues to be damaged by Defendants’ infringement of the ’277 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

63. Defendants’ conduct in infringing the ’277 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

COUNT II

Infringement Of The ’720 Patent

64. Ravgen incorporates by reference paragraphs 1–63.

65. The ’720 Patent is valid and enforceable.

66. Defendants have infringed, and continue to infringe, one or more claims of the ’720 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including Defendants’ Myriad Prenatal Screens.

67. As one example, Defendants infringe at least claim 1 of the '720 patent by using the Myriad Prenatal Screens. For example, use of the Myriad Prenatal Screens requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 33 at 334 (Dale Muzzey, *et al.*, *Noninvasive prenatal screening for patients with high body mass index: Evaluating the impact of a customized whole genome sequencing workflow on sensitivity and residual risk*, 40 PRENATAL DIAGNOSTICS 333, 334 (2020) ("NIPS directly interrogates cfDNA extracted from maternal plasma . . . . [This] study included 58,105 patients who underwent WGS-based NIPS over an 8-month period with the Prequel Prenatal Screen . . . .").);

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (*see, e.g.*, Ex. 28 (https://myriadwomenshealth.com/how-to-10ml-blood/).); Ex. 29 (https://help.myriadwomenshealth.com/s/article/000016237) (Question: "How are samples collected for the Prequel Prenatal™ Screen?" Answer: "A sample is collected from a pregnant patient who is at least 10 weeks . . . into her pregnancy . . . . Specifically, Myriad Women's Health requires one 10mL Streck tube . . . ."); Ex. 31 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA BCTs as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell***

lysis"));

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 32 (https://s3.amazonaws.com/static.counsyl.com/website/PDFs/posters/12.+Avoiding+Unnecessary+Trade-Offs+Clinical+Experience+for+a+Noninvasive+Prenatal+Screen.pdf) ("Chromosome analysis results were reported as no aneuploidy detected ("negative"), aneuploidy detected ("positive"), or aneuploidy suspected (also "positive").); Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/) ("For Prequel, the patient will contact Client Services to discuss blood collection options and the phlebotomist will send the specimen to Myriad for processing.")).

68. Defendants have infringed, and continue to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the Myriad Prenatal Screens either themselves and/or by directing and/or controlling the performance of the claimed steps by third-party laboratories performing the Myriad Prenatal Screens. For example, Defendants use the Myriad Prenatal Screens by collecting and analyzing samples sent to Defendants' laboratories for processing. (*See, e.g.*, Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/) ("For Prequel, the patient will contact Client Services to discuss blood collection options and the phlebotomist will send the specimen to Myriad for processing."); Ex. 35 (https://myriadwomenshealth.com/our-science/) ("As one of the pioneers in clinical next generation sequencing (NGS) and one of the largest sequencing facilities in the world, Myriad Women's Health's CLIA laboratory has tested over one million samples.").) On information and belief, Myriad has the right and the ability to direct and

control the activities of MWH in several ways, including through Myriad's 100% ownership of MWH, through instituting programs and measures (such as policies or protocols) at MWH, and through interim instructions via at least Myriad's employees and/or officers who hold leadership roles at MWH. Further, MWH acts on behalf of Myriad, including when MWH performs tests on Myriad's behalf for Myriad's patients, or provides test results to health care providers and/or patients on Myriad's behalf.

69. In addition or in the alternative, Defendants have also induced infringement, and continue to induce infringement, of one or more claims of the '720 Patent under 35 U.S.C. § 271(b). Defendants actively, knowingly, and intentionally induce infringement of the '720 Patent by selling or otherwise supplying the Myriad Prenatal Screens with the knowledge and intent that third-party laboratories will use the Myriad Prenatal Screens supplied by Defendants to infringe the '720 Patent. Defendants act with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Myriad Prenatal Screens and/or the creation and dissemination of supporting materials, instructions, product manuals, and/or technical information related to the Myriad Prenatal Screens.

70. Defendants specifically intend and are aware that the ordinary and customary use of the Myriad Prenatal Screens would infringe the '720 Patent. For example, Defendants sell and provide the Myriad Prenatal Screens, which when used in their ordinary and customary manner intended and instructed by Defendants, infringe one or more claims of the '720 Patent, including at least claim 1. On information and belief, Defendants further provide product manuals and other instructional materials that cause their customers and partners to operate the Myriad Prenatal Screens for their ordinary and customary use. (*See, e.g.*, Ex. 34 (https://myriadwomenshealth.com/prenatal-virtual-ordering/); Ex. 28

(https://myriadwomenshealth.com/how-to-10ml-blood/).) Defendants accordingly induce third parties to use the Myriad Prenatal Screens in their ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

71. In addition or in the alternative, Defendants contribute to the infringement by third parties, such as health care providers or laboratories, of one or more claims of the '720 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the Myriad Prenatal Screens, knowing that those products constitute a material part of the inventions of the '720 Patent, knowing that those products are especially made or adapted to infringe the '720 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

72. Defendants have had knowledge of and notice of the '720 Patent and their infringement since at least the launch date of each of the infringing products.

73. Defendants' infringement of the '720 Patent has been, and continues to be, willful and deliberate since at least the launch date of each of the infringing products.

74. Ravgen has been and continues to be damaged by Defendants' infringement of the '720 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

75. Defendants' conduct in infringing the '720 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Ravgen prays for judgment as follows:

A. That Myriad and MWH have infringed each of the Patents-in-Suit;

B. That Defendants' infringement of each of the Patents-in-Suit has been willful;

C. That Ravgen be awarded all damages adequate to compensate it for Defendants' past infringement and any continuing or future infringement of the Patents-in-Suit up until the date such judgment is entered, including pre- and post-judgment interest, costs, and disbursements as justified under 35 U.S.C. § 284;

D. That any award of damages be enhanced under 35 U.S.C. § 284 as result of Defendants willful infringement;

E. That this case by declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Ravgen be awarded the attorney fees, costs, and expenses incurred in connection with this action;

F. That Ravgen be awarded either a permanent injunction, or, at least, a compulsory ongoing licensing fee; and

F. That Ravgen be awarded such other and further relief at law or equity as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff Ravgen hereby demands a trial by jury on all issues so triable.

Dated: December 21, 2020

Respectfully submitted,

FARNAN LLP

/s/ Michael J. Farnan

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